glycol) is mixed with the Solutol HS 15 and the active ingredient is dissolved therein whilst stirring. A fatty acid mono-, di- and triester, a glyceride of ricinoleic acid and/or a thickener is optionally added to the solution.

[0082] The preparations obtained are subsequently filled for example in liquid form into hard or soft gelatin capsules of the desired size, in the desired concentration. The compositions may also be further processed in known manner into tablets. To this end, as described in example 3, the active ingredient is dissolved in a mixture of Solutol HS 15 and castor oil. The solution thus produced is added whilst stirring to the molten component Cutina MD. The liquid melt is poured out, and after solidifying is pulverized in a sifting machine. The granulates obtained are mixed with conventional excipients such as lubricants and liniments, disintegrants, fillers, flavourings etc., and the mixtures pressed into tablets with the desired content of cyclosporin; an example of a conventional excipient is silicon dioxide available commercially under the trade mark Aerosil (Degussa, Germany). If required, the tablets may be coated with specifically desired coatings to improve taste, for aesthetic reasons or to control release of the active ingredient in the intestines, e.g. to control gastric juice resistance or solubility in the small intestine.

[0083] Similarly, the liquid melts may be directly filled into blisters.

[0084] A group of beagles was used for the experiments and to compare the bioavailability values of the capsule preparations according to the invention. The test preparations were applied perorally to fasted animals using stomach tubes. Blood was taken from the vena saphena of the animals at pre-determined time intervals, and collected in appropriate plastic tubes with an addition of EDTA. The blood samples were stored at −18° C. until used for evaluations. The cyclosporin evaluation was made in whole blood by means of fluorescence polarisation immunoassay (FPIA).

[0085] The areas under the curves (AUC), in which the blood levels of the active ingredient are plotted against time, were calculated according to the trapeze rule. The average AUC values of the compositions according to the invention are illustrated in the following table, in a comparison with the commercial preparation of cyclosporin capsules (Sandimmun® Optoral), which were determined in the same reproducible way, at the same dosage, using the same dogs.

Examples	AUC (0–12 h) ng/ml
1	26.555 ± 7.195
2	24.832 ± 10.206
3	17.828 ± 8.193
4	33.109 ± 11.504
cyclosporin capsules (comparison) (Sandimmun ® Optoral) preparation for comparison	25.469 ± 12.086

[0086] As the above bioavailability tests show, it is possible using the pharmaceutical compositions according to the invention to make the active ingredient cyclosporin orally available in such a form that its bioavailability corresponds at least to the well known preparations.

[0087] It is especially surprising to the person skilled in the art that, in accordance with the invention, only three to at most four excipients and carriers, as well as solubilisers, are sufficient to attain the desired bioavailability. This formulation with very few excipients, which is simplified compared with the preparation for comparison (which contains 6 different components), not only reduces the incompatibilities, but also increases safety of the medicament during production, storage and administration. The latter advantage is especially notable compared with the concentrates known from DE-B-39 24 207, which can only be prepared outside the pharmaceutical industry "in situ" into the dosage form ready for injection, whereby as a result of the required final dilution with special solutions, there is a danger of inaccurate dosages, insterility etc.

[0088] With the composition according to the invention, the applicants have succeeded in making available a compact dosage form, for example tablets, with a cyclosporin content, i.e. a medicinal form, which is easy to produce, to handle and to administer, and in addition is economical to produce.

[0089] Encapsulation of the formulations into soft gelatin or hard gelatin capsule preparations is effected in conventional manner or by using the process for soft gelatin capsules as described in EP 649651. In a stress test at temperatures of −18° C. to 60° C., the preparations according to the invention did not show any precipitation, decomposition or other changes even after storage for 6 months.

[0090] All known natural and synthetic cyclosporins, including the analogues and derivatives thereof, are suitable for use in the preparations according to the invention. Examples of such cyclosporins may be found for example in DE-OS 40 03 844 and DE-OS 40 05 190. Cyclosporin A is preferred.

[0091] Compositions containing ([3'-desoxy-3'-oxo-MeBmt]^{1}-[Val]^{2}-Ciclosporin) instead of Cyclosporin A may be prepared in analogous manner to the compositions described in Examples 1 to 4 above.

[0092] Compositions containing as active agent rapamycin, 40-0-(2-hydroxy)ethyl rapamycin, 32-deoxorapamycin, 16-pent-2-ynyloxy-32(S)-dihydrorapamycin, 33-epi-chloro-33-desoxy-ascomycin, FK506, the compound disclosed under Example 6d and Example 71 in EP 569 337, or the compound disclosed under Example 8 in EP 626 385 instead of cyclosporin A may be prepared in analogous manner to the compositions described in Examples 1 to 4 above. If desired, the Aerosil may be omitted. The compositions may be encapsulated in soft gels and are stable over, e.g. 2 years.

[0093] The concentration of active ingredient in the oral form of administration according to the invention is 20 to 200 mg, preferably 50 to 100 mg per unit dose. References to weight of composition as used herein ignore the weight of any encapsulating medium, e.g. softgel capsule shell.

1. Pharmaceutical composition for peroral administration comprising

(a) a cyclosporin or macrolide as active ingredient, and

(b) a polyethoxylated saturated hydroxy-fatty acid.

2. A composition as claimed in claim 1 containing additionally

(c) a C_2-C_3-alcohol having one or two hydroxy groups.